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(21) International Application Number: PCT/US98/20904 (22) International Filing Date: 5 October 1998 (05.10.98) (30) Priority Data: 60/060,995 3 October 1997 (03.10.97) US (71) Applicant: UNIVERSITY OF MASSACHUSETTS [US/US]; 26th floor, 1 Beacon Street, Boston, MA 02108 (US). (72) Inventors: DAVIS, Roger, J.; 53 Hickory Drive, Princeton, MA 01541 (US). FLAVELL, Richard, A.; Guilford, CT 06437 (US). RAKIC, Pasko; New Haven, CT (US). WHITMARSH, Alan, J.; Shrewbury, MA 01545 (US). KUAN, Chia-Yin; Wallingford, CT (US). YANG, Di; Hamden, CT 06514 (US). (74) Agent: FASSE, J., Peter, Fish & Richardson P.C., 225 Franklin Street, Boston, MA 02110-2804 (US).		(81) Designated States: AU, CA, JP, KR, European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE). Published <i>With international search report.</i>
(54) Title: JNK3 MODULATORS AND METHODS OF USE (57) Abstract The c-Jun NH ₂ -terminal kinase (JNK) group of MAP kinases are activated by exposure of cells to environmental stress. The role of JNK in the brain was examined by targeted disruption of the gene that encodes the neuronal isoform JNK3. It was found that JNK3 is required for the normal response to seizure activity. Methods of screening for molecules and compounds that decrease JNK3 expression or activity are described. Such molecules or compounds are useful for treating disorders involving excitotoxicity such as seizure disorders, Alzheimer's disease, Huntington disease, Parkinson's disease, and ischaemia.		

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US98/20904

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) : C12N 15/00, 15/09, 15/63, 5/00; A01N 43/04; A61K 31/70

US CL : 800/18, 21, 22, 25; 435/455, 463, 4, 6, 7; 514/44, 2

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 800/18, 21, 22, 25; 435/455, 463, 4, 6, 7; 514/44, 2

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

Please See Extra Sheet.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	GUPTA et al. Selective Interaction of JNK Protein Kinase Isoforms with Transcription Factors. The EMBO Journal. 1996, Vol. 15, No. 11, pages 2760-2770, see entire document.	1-17
Y	YANG et al. Targeted Disruption of the MKK4 Gene Causes Embryonic Death, Inhibition of c-Jun NH2-Terminal Kinase Activation, and Defects in AP-1 Transcriptional Activity. Proceedings of the National Academy of Sciences, USA. April 1997, Vol. 94, pages 3004-3009, see entire document.	1-17



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents:	*T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
A document defining the general state of the art which is not considered to be of particular relevance	*X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
B earlier document published on or after the international filing date	*Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	*A* document member of the same patent family
O document referring to an oral disclosure, use, exhibition or other means	
P document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

21 DECEMBER 1998

Date of mailing of the international search report

14 JAN 1999

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International application No.

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C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	LANDER et al. Differential Activation of Mitogen-Activated Protein Kinases by Nitric Oxide-related Species. The Journal of Biological Chemistry. 16 August 1996, Vol. 271, No. 33, pages 19705-19709, see entire document.	1-17
A	LO et al. Reactive Oxygen Species Mediate Cytokine Activation of c-Jun NH2-Terminal Kinases. The Journal of Biological Chemistry. 28 June 1996, Vol. 271, No. 26, pages 15703-15707, see entire document.	1-17
A	CARBONI et al. Localization of the Messenger RNA for the c-Jun NH2-terminal Kinase Kinase in the Adult and Developing Rat Brain: an In Situ Hybridization Study. Neuroscience. September 1997, Vol. 80, No. 1, pages 147-160, see entire document.	1-17
A, E	GOMEZ et al. JNK (c-Jun NH2-Terminal Kinase) is a Target for Antioxidants in T Lymphocytes. Journal of Biological Chemistry. 18 October 1998, Vol. 271, No. 42, pages 26335-26340, see entire document.	1-17

INTERNATIONAL SEARCH REPORT

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B. FIELDS SEARCHED

Electronic data bases consulted (Name of data base and where practicable terms used):

MEDLINE, CAPLUS, BIOSIS, EMBASE, WPIDS, APS

search terms: cJun NH terminal kinase, jnk3, map kinase, neurons, brain, seizure, screen, indentify, knockout, mouse, mice, disrupt, target, embryonic stem cell